



POLYTECHNIC UNIVERSITY OF THE PHILIPPINES  
COLLEGE OF SCIENCE - DEPARTMENT OF BIOLOGY  
Bachelor of Science in Biology Major in Microbiology



**UNVEILING THE POTENTIAL DRUG LIGANDS  
AGAINST THE VIRULENCE-RELATED HYPOTHETICAL  
PROTEIN IN *Cryptococcus neoformans*:  
AN *IN SILICO* ANALYSIS APPROACH**

**AUTHORS**

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Review

## Neglected fungal zoonoses: hidden threats to man and animals

S. Seyedmousavi<sup>1, 2, 3</sup> ✉, J. Guillot<sup>4</sup>, A. Tolooe<sup>5</sup>, P.E. Verweij<sup>2</sup>, G.S. de Hoog<sup>6, 7, 8, 9, 10</sup>

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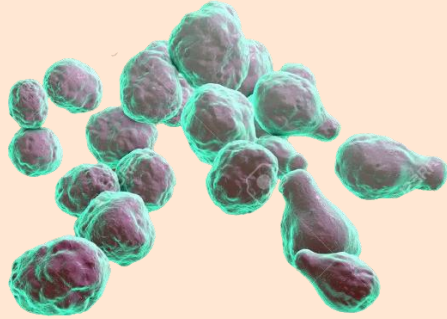
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<i>Cryptococcus neoformans</i> , <i>Cryptococcus gattii</i>	Cryptococcosis	Worldwide	Mainly by inhalation of fungus, occasionally through breaks in the skin	Wide variety of mammals, birds, reptiles and amphibians
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<i>Penicillium (Talaromyces) marneffeii</i>	Penicilliosis	Southern China and South-East Asia	Unknown	Bamboo rats, domestic animals such as dogs, cats
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# *Cryptococcus neoformans*

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**3<sup>rd</sup> most invasive  
fungal pathogen.**



**Half million  
Deaths**



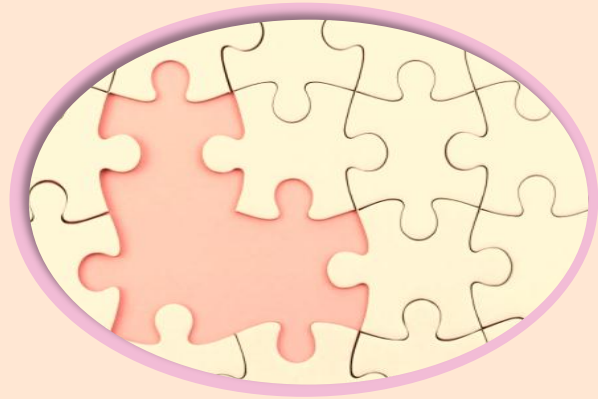
**2<sup>nd</sup>  
opportunistic  
infection.**



Sources:

Salyer, et al. (2017) <https://doi.org/10.3201/eid2313.170418>; CDC (2017) <https://www.cdc.gov/onehealth/basics/zoonotic-diseases.html>  
Seyedmousavi et al. (2015) doi:10.1016/j.cmi.2015.02.031;Kainz et al. (2020) <https://doi.org/10.15698/mic2020.06.718>

# HYPOTHETICAL PROTEINS



**Predicted to exist.**

**“Unknown”, “uncharacterized”, and “hypothetical” in terms of their biological functions. (Pranavathiyani et al., 2020).**

**Identify and characterize the potential drug ligands associated with the hypothetical proteins in *C. neoformans* through *in silico* analysis.**

## Stage 1

Evaluate  
NCBI  
UNIPROT  
BLAST2GO  
HMMSCAN

Dedicated to  
Filter the non-  
performing  
redundant  
proteins

## Stage 2

### Phase 1

Determine  
the  
DRUGBANK  
GENE  
ONTOLOGY  
KEGG  
PATHWAYS

To choose  
12 Candidate  
Hypothetical  
Proteins

### Phase 2

Identify the  
HOMOLOGY  
MODEL  
Q-MEAN  
PROSAWEB  
PROCHECK  
PPI

To denote  
ONE CHOSEN  
HYPOTHETIC-  
AL PROTEIN

### Phase 3

Identify the  
PROPERTIES  
OF THE  
PROTEIN  
PROPERTIES  
OF THE  
LIGANDS

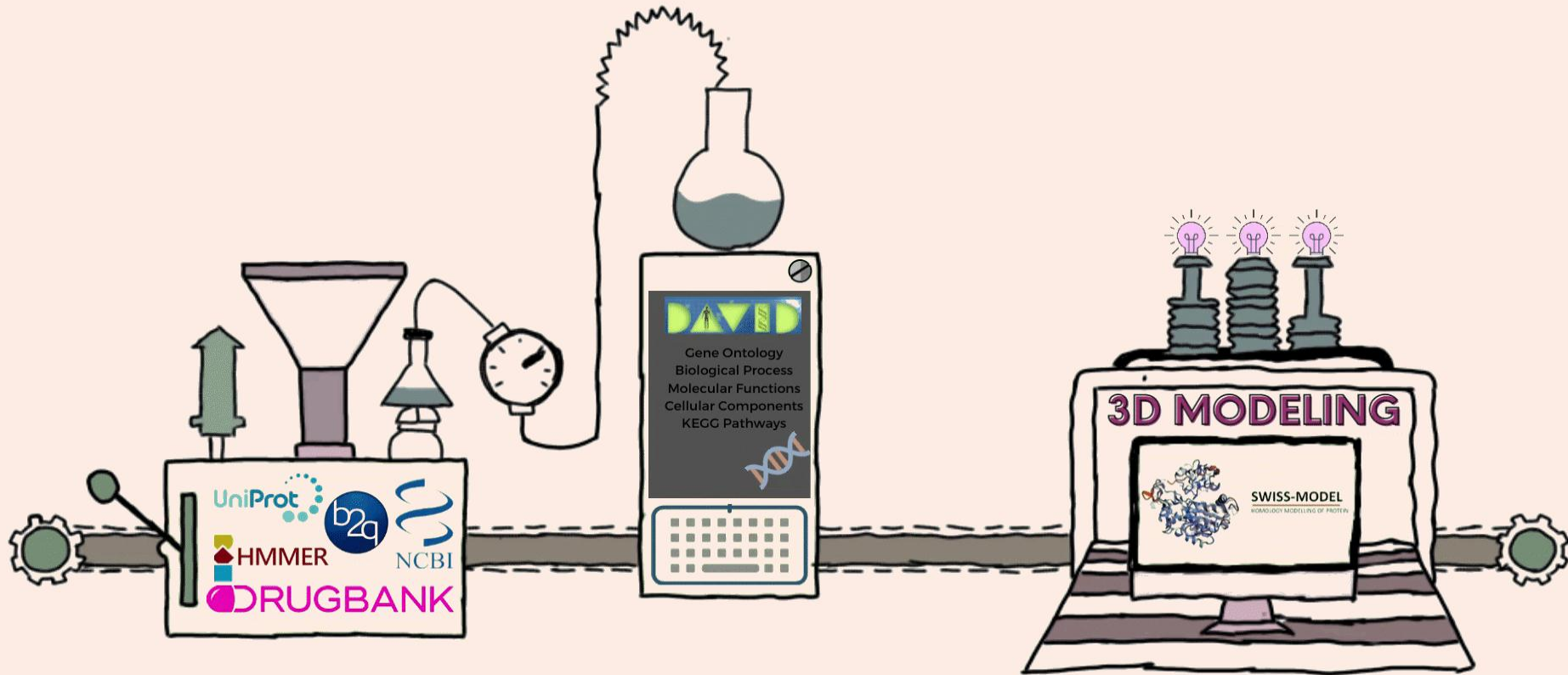
MegaX  
ProtParam  
NetSurfP  
Interpro  
Wolf Psort  
SOSUI  
PubChem  
SWISS  
PkCSM  
Pass Online

## Stage 3

Use the  
AutoDock Tools  
Autodock Vina  
Biovia Discovery  
Studio

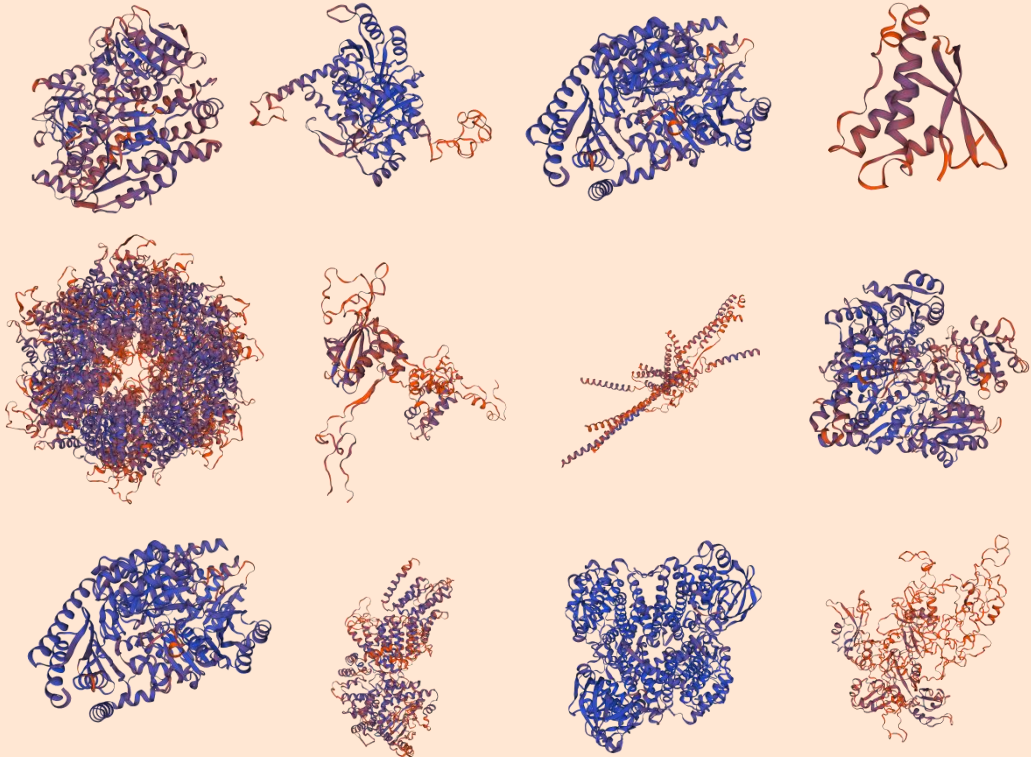
To analyze the  
Protein-  
Ligand  
Interaction

# Screening of the Hypothetical Proteins





# Validation of the homology models



**Procheck**

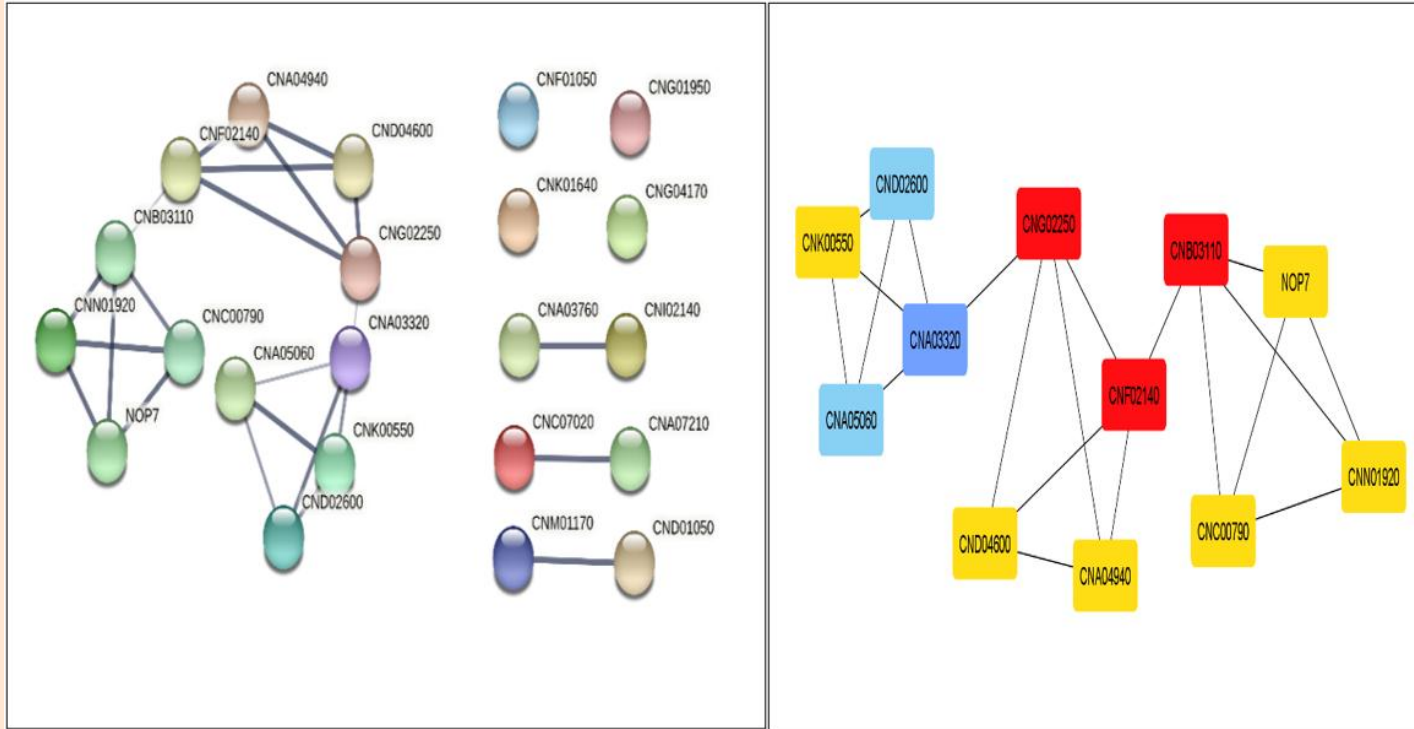


**Prosa-web**

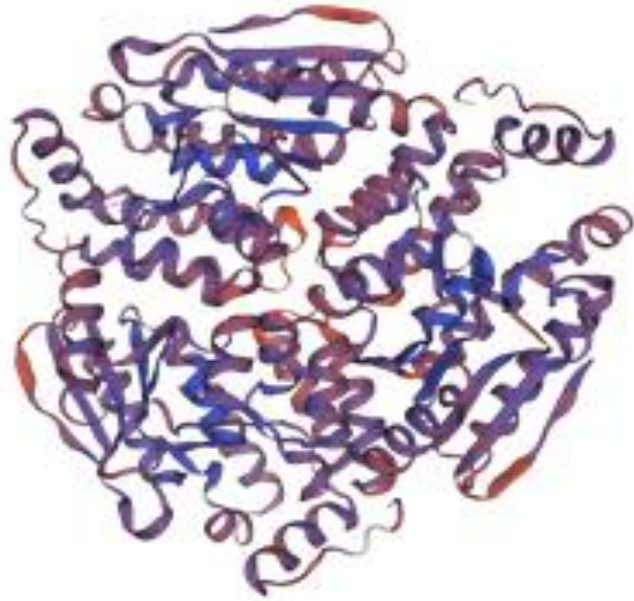


**Q-mean**

# Protein-protein Interaction



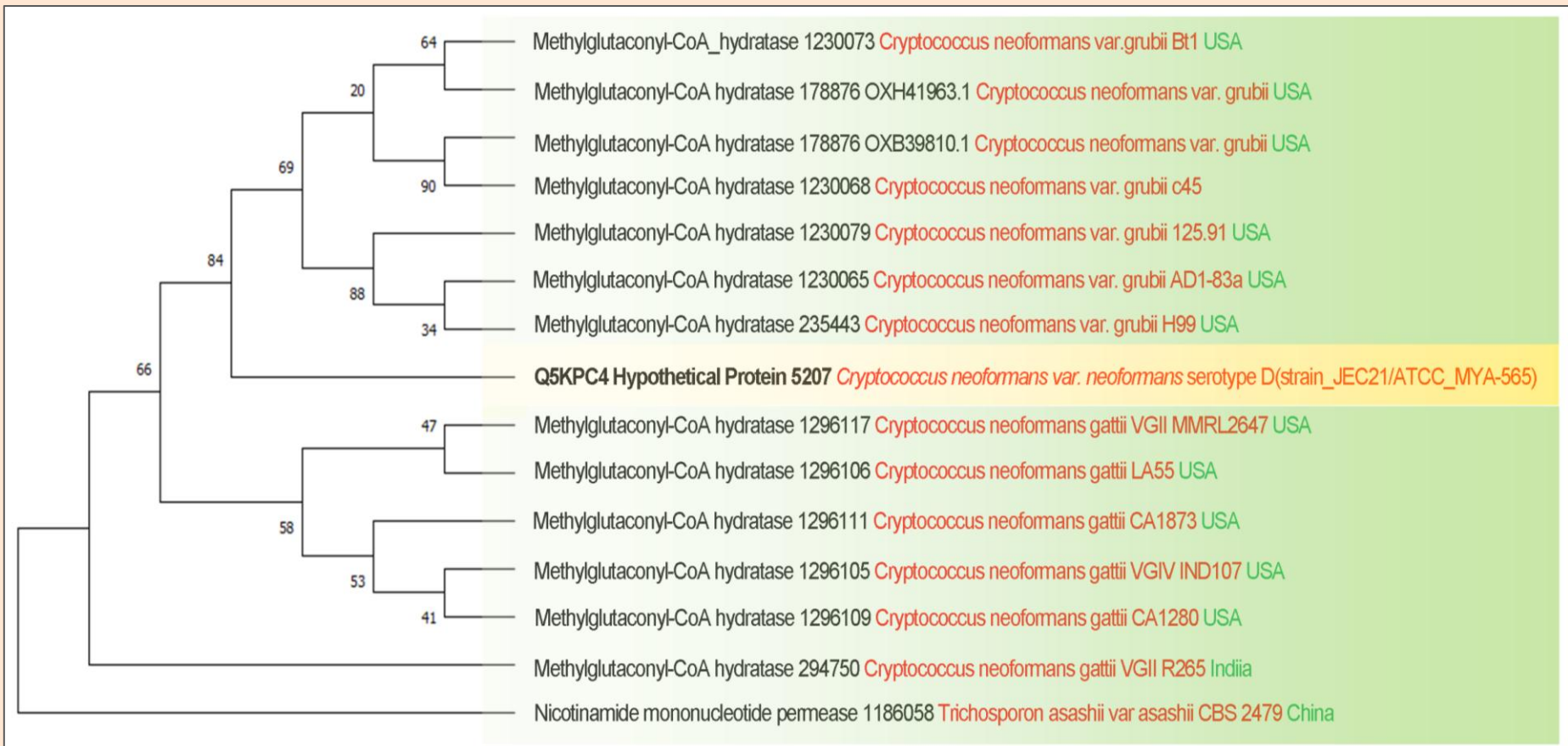
**Protein-Protein Interactions and Hubgenes of the 12 chosen Hypothetical Protein**  
**(a) PPI network constructed with STRING; (b) Network of hub genes.**



**Q5KPC4**

## CHARACTERISTICS

- Basic in nature (ProtParam).
- High thermostability (ProtParam).
- Alpha helices as the prominent protein structure (NetSurfP).
- Soluble (SOSUI server).
- Mitochondrial protein (Wolf Psort).



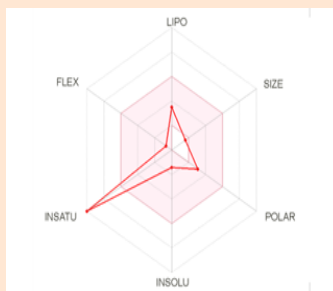
**Phylogenetic Tree of the Q5KPC4 and 12 identical proteins based on BlastP results using Maximum Likelihood Algorithm, with Nicotinamide mononucleotide permease from *Trichosporon asashii* as an outgroup.**



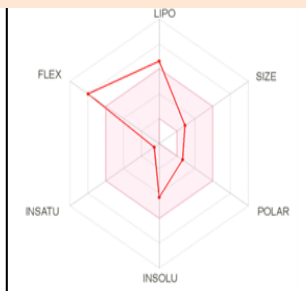
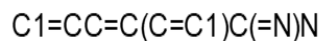
## Q5KPC4 belongs to:

- ✓ **1,4-dihydroxy-2-naphthoyl-CoA synthase (ECH\_1) and enoyl-CoA hydratase/isomerase (ECH\_2) family.**
- ✓ Homologous superfamily **crotonase (ClpP)**
- ✓ Conserved sites (**enoyl-CoA hydratase**)
- ✓ Unintegrated regions (**enoyl-CoA hydratase-related**).

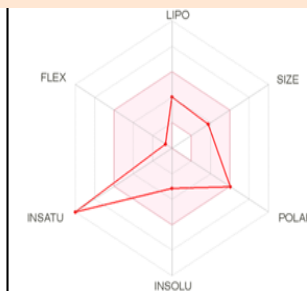
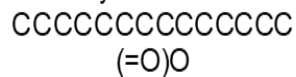
**Determination of the domain through a.) Pfam and b.) Interpro**



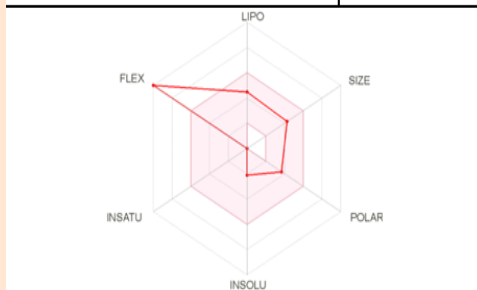
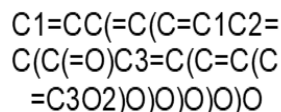
**Benzamidine**



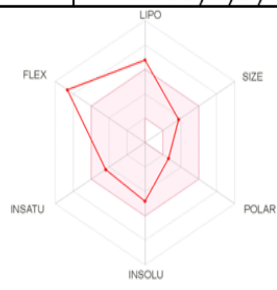
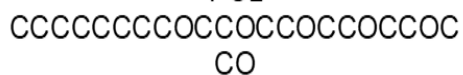
**Myristic acid**



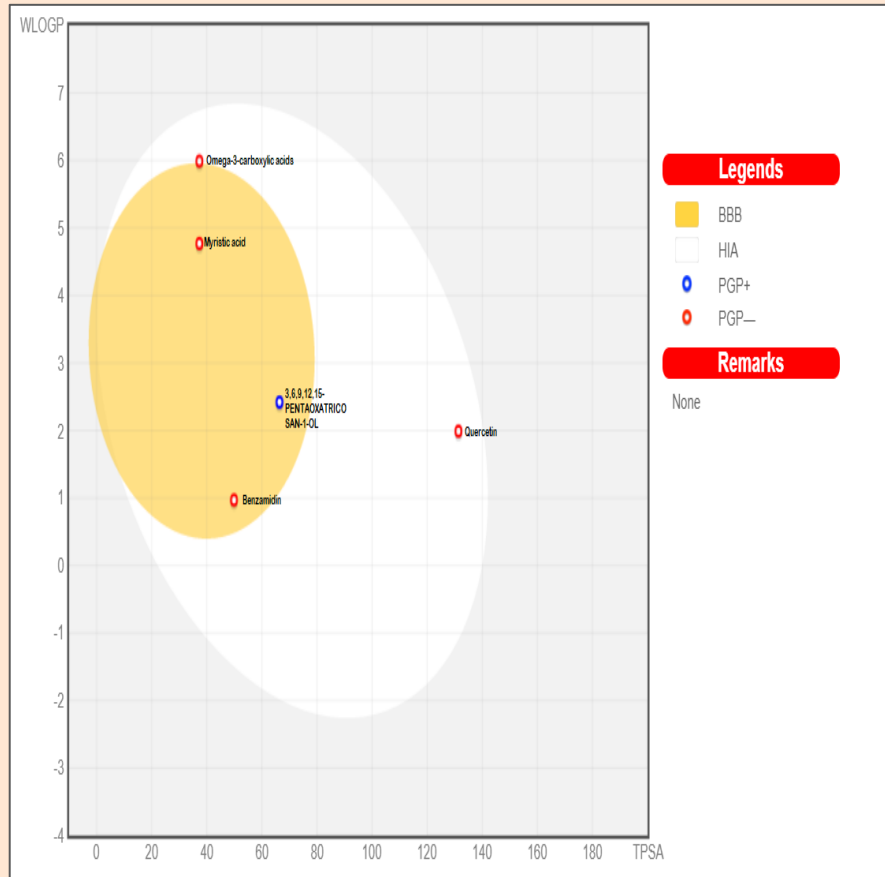
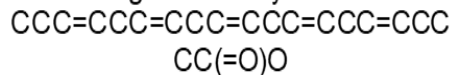
**Quercetin**



**3,6,9,12,15-Pentacosan-1-ol**

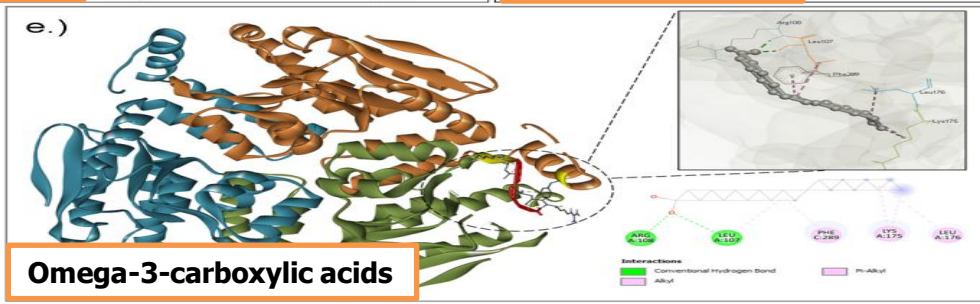
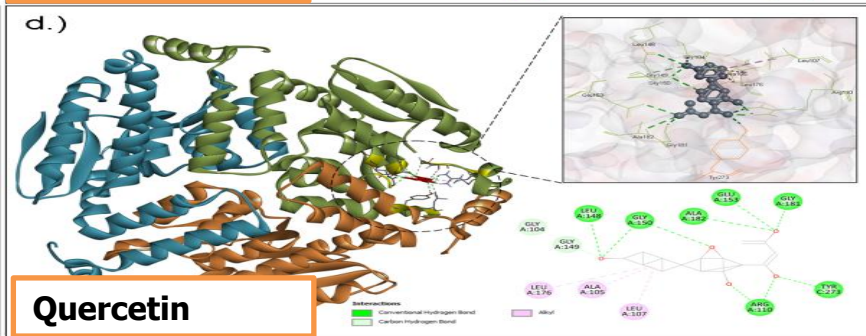
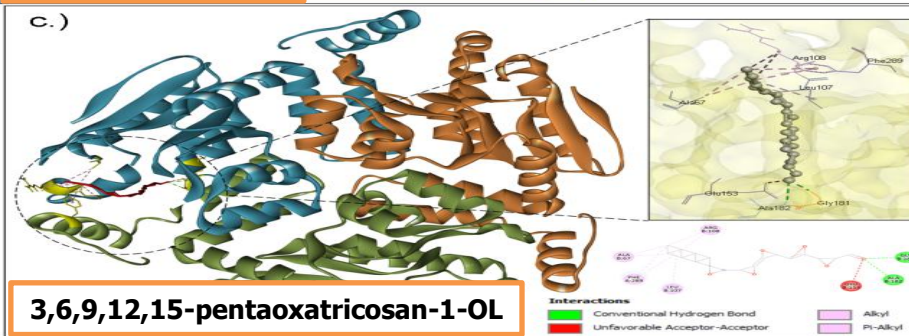
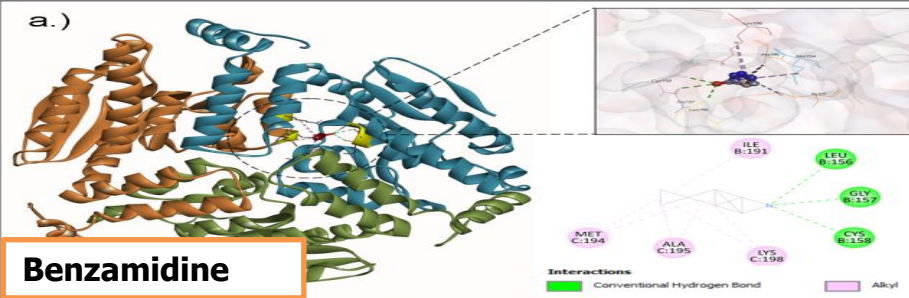


**Omega-3-carboxylic acids**



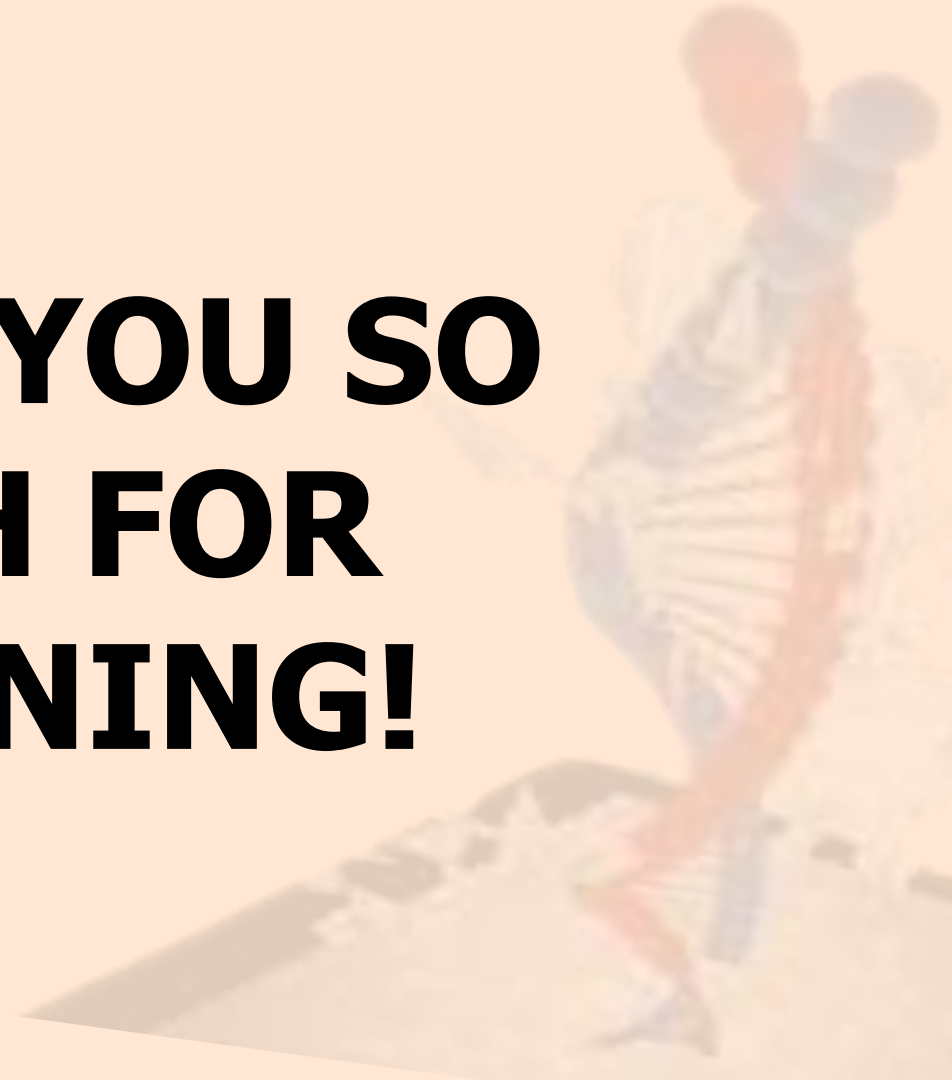
**Radar plots for the five promising ligands of Q5KPC4.**

**BOILED-Egg plot of the five potential drug ligands.**



# Molecular docking of the 5 ligands and Q5KPC4

**THANK YOU SO  
MUCH FOR  
LISTENING!**







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